Attorney Docket No.: ALX-149 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#18 03/31/99

Applicant : Yi Wang and Louis Matis

Serial No.: 08/311,489 ⇒ 09/667612

Filed : September 23, 1994

For : METHODS FOR THE TREATMENT OF INFLAMMATORY JOINT DISEASE

Examiner : F. C. Eisenschenk, Ph.D.

Group : 1816

Commissioner of Patents and Trademarks
Washington, D.C. 20231

DECLARATION OF YI WANG PURSUANT TO 37 C.F.R. § 1.132

Sir:

I, Yi Wang, hereby declare that:

1. I am an inventor of the invention claimed in the above-identified application and have read the office action in the application dated December 14, 1995 and am familiar with Sindelar et al. (U.S. Patent 5,173,499) which was cited by the Examiner in that office action.

2. I received my M.D. from the Beijing Medical University, Beijing, China, in 1983. I spent the following two years doing clinical work and taking advanced courses in Beijing. In 1985, I came to the United States as a postdoctoral researcher and have been involved in the study of autoimmune disease pathogenesis since that time. Since 1993 I have been a research scientist at

Alexion Pharmaceuticals, Inc. the assignee of the above referenced application. My current title is Senior Research Scientist.

3. In order to effectively carry out my job it is important that I keep up with the scientific literature dealing with autoimmune diseases. In particular, since 1993 I have been familiar with the scientific literature regarding the roles of complement and of T cells in the pathogenesis of inflammatory joint disease.

4. I understand that the Examiner has rejected Claims 11-13 of the above-referenced application and asserted that it would be obvious to treat established joint inflammation in accordance with the methods encompassed by those claims. I further understand that the Sindelar et al. patent referred to in paragraph 1 above was cited by the Examiner in these rejections. I believe that the Sindelar et al. patent would not have led someone familiar with the scientific literature regarding the role of complement in the pathogenesis of inflammatory joint disease to reasonably expect that any of the methods claimed in the above referenced application would be successful in treating established joint inflammation. In particular, it was known that animals carrying a genetic defect such that they produced no C5 can still develop established joint inflammation. (See, for example, Andersson et al., 1991, Reference No. 6, modified 1449 form; and Banerjee et al., 1989, Reference No. 8, modified 1449 form, both of which report that established joint inflammation occurred in the absence of complement C5 activity.) In fact, as discussed below, at the time that experiments demonstrating the efficacy of the methods of

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the invention claimed in the above referenced application (i.e., the work reported in Example 1 of the above referenced application) were being planned, I did not myself expect that such methods would be successful.

5. On May 2, 1994, prior to starting the work reported in Example 1 of the above referenced application, I reported on my ongoing studies of prevention of inflammatory joint disease to the Scientific Advisory Board of my employer, Alexion Pharmaceuticals, Inc., the assignee of that application. My report included a review of preliminary data obtained in studies of prophylactic treatment of animals with a C5 blocker prior to the onset of joint inflammation, which studies are described (and more fully developed data presented) in the Examples and Figures of the above referenced application (see, for instance, Example 2 and the Figures cited therein). The preliminary prophylaxis results showed such an unexpectedly dramatic effect in inhibiting the development of joint inflammation that experiments to test the effects of C5 blockade on established inflammation were planned.

6. While describing these results and plans to the members of the Scientific Advisory Board on May 2, 1994, I predicted that, in spite of the surprising efficacy of C5 blocker administration in prophylaxis, C5 blocker administration would not be effective in treating established joint inflammation, and that anti-T cell treatments would be required for effective treatment. This prediction was based upon my understanding of the knowledge in the art at the time, and in particular upon my knowledge, discussed in paragraph 4, above, that animals that had a genetic defect such

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that they produced no C5 are still susceptible to established joint inflammation.

7. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Yi Wang

Yi Wang, M.D.

Signed at New Haven, Connecticut

this 11 day of September, 1996.